REMARKS

Entry of the foregoing, reexamination and reconsideration of the above-identified application are respectfully requested.

Claims 37-48 have been cancelled by this amendment without prejudice or disclaimer. This amendment is being made to expedite prosecution of the remaining claims, and applicants reserve the right to pursue the cancelled claims in a continuation application.

Applicants note with appreciation the indication that claims 49-52 are free of the prior art. Claims 49, 50 and 52 have been ameneded to be independent claims. These claims, at the very least, are thus believed to be in condition for allowance.

Claim 24 has been amended to recite within the body of the claim that the reagent is delivered into the nucleoplasm of a cell. That the reagent is delivered to the nucleoplasm is thus clearly a required element of the claim.

New claims 53-65 have been added. These claims recite a "method of detecting a reagent in a nucleoplasm of a cell," and further require a step of "detecting said reagent in the nucleus of said cell" after penetration of the complex into the nucleoplasm of the cell. In view of the indication that claims that "require the specific step of detecting label in the nucleus" are allowable, these claims are believed to also be allowable.

The Official Action states that claims 49-52 are free of the prior art "because they require the specific step of detecting label in the nucleus." New claims 53-65 also require similar steps. In view of this prior indication, at the very least, claims 49-65 are believed to be in condition for allowance.

Claims 37-40 were rejected under 35 U.S.C. §112, first paragraph. This rejection is rendered moot by the cancellation of these claims.

Claims 24, 26-30, 32, 34-39 and 41-47 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Sabharwal et al in view of Johnstone and Thorpe, and also in view of Goers. This rejection is respectfully traversed.

The pending claims now at issue in this rejection are claims 24, 26-30, 32, and 34-36. The Official Action asserts that the claims "are drawn to methods of combining MAL with a reagent to form a complex and applying the reagent to cells." Page 4. However, the claims now pending are directed to a "method for delivering a reagent into the nucleoplasm of a cell, wherein said cell is susceptible to an oligomeric form of α-lactalbumin (MAL), said method comprising combining said reagent with MAL to form a complex, and applying said complex to the cells." Such a method is neither disclosed nor suggested by the cited art.

Sabharwal is cited as teaching that MAL has antiadhesive properties in certain bacterial strains. Johnstone and Thorpe or Goers is cited as teaching labeling proteins with radioactive labels or biotin. *See,* Page 5. These teachings, however, fail to overcome or remedy the failure of the primary reference, Sabharwal, in teaching or suggesting a method as claimed. None of the cited art discloses or even suggests that MAL in combination with a reagent could be used to deliver the reagent into the nucleoplasm of a cell. There is no teaching or suggestion in Sabharwal that MAL will enter the nucleoplasm of a cell. Nor is there any suggestion to combine MAL with any reagents. The secondary references are unrelated to targeting the nucleoplasm of cells with reagents in general, or more specifically, using MAL to target the nucleoplasm. Thus, there would be no motivation for one skilled in the art to combine MAL with a reagent in order to deliver the reagent into the nucleoplasm of the cell. Nor does the cited combination in any way disclose or even suggest a method for targeting the nucleoplasm of a cell, as instantly claimed.

In view of the above, withdrawal of the rejection of record is respectfully requested and believed to be in order.

Claims 24-30, 32-39 and 41-45 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Hakansson et al in view of Johnstone and Thorpe, and also in view of Goers. This rejection is respectfully traversed.

Hakansson is said to teach that MAL causes apoptosis in tumor cells and teaches applying MAL to cells. It allegedly would have been obvious to combine MAL with a reagent useful in detection to quantify uptake of MAL in tumor cells or to determine the specificity of MAL uptake. Hakansson in combination with the secondary references, however, fails to disclose or even suggest a method as instantly claimed.

The pending claims now at issue in this rejection are claims 24-30 and 32-36. These claims are directed to a "method for delivering a reagent into the nucleoplasm of a cell, wherein said cell is susceptible to an oligomeric form of α-lactalbumin (MAL), said method comprising combining said reagent with MAL to form a complex, and applying said complex to the cells." Such a method is neither disclosed nor suggested by the cited art. Hakansson et al does not teach or suggest that MAL can enter the nucleoplasm of a cell. Nor does Hakansson et al teach or suggest combining MAL with any other reagent in general, or more specifically a reagent for delivery into the nucleoplasm of a cell.

The secondary references fail to overcome or remedy these deficiencies. There is no teaching of combining the reagents with any other agent in order to target their delivery. Nor is there any teachings of targeting reagents into the nucleoplasm of a cell.

In view of the above, the cited art does not render obvious the claims of record. Withdrawal of the rejection of record is respectfully requested and believed to be in order.

Claims 24 and 31 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Hakansson et al or Sabharwal et al in view of Robinett. This rejection is respectfully traversed.

On page 7, the Official Action states that the claims are "drawn to methods comprising combining MAL with a reagent to form a complex, applying the complex to cells, wherein the reagent is polypeptide or protein fused to MAL." However, the claims are directed to methods for "delivering a reagent into the nucleoplasm of a cell." As stated *supra*, neither Hakansson et al nor Sabharawl teaches or suggests a method for delivering a reagent into the nucleoplasm of a cell in general, or more specifically, by combining the reagent with MAL to form a complex. Neither reference teaches or suggests combining the MAL with any other reagent or that MAL will enter the nucleoplasm of a cell.

Robinett fails to overcome or remedy these deficiencies of the primary references. Robinett does not disclose or suggest combining fluorescent proteins with MAL and also does not teach or suggest that the combination could be uded to enter the nucleoplasm of a cell. The combination of Robinett with Hakansson et al or Sabharwal et al thus fails to render obvious the claimed invention.

In view of the above, withdrawal of the rejection of record is respectfully requested and believed to be in order.

Claims 37-41, 44, 45 and 48 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Hakansson et al in view of Mattes. This rejection has been rendered moot by the cancellation of these claims. Withdrawal of the rejection is thus respectfully requested and believed to be in order.

Claim 48 has been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Hakansson et al in view of Goldenbery. This rejection has been rendered moot by the

cancellation of this claim. Withdrawal of the rejection is thus respectfully requested and believed to be in order.

It is respectfully submitted that all rejections have been overcome by the above amendments. Thus, further and favorable action in the form of a Notice of Allowance is respectfully requested.

In the event that there are any questions relating to this amendment or the application in general, it would be appreciated if the Examiner would contact the undersigned attorney by telephone at (650) 622-2360 so that prosecution of the application may be expedited.

Respectfully submitted,
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